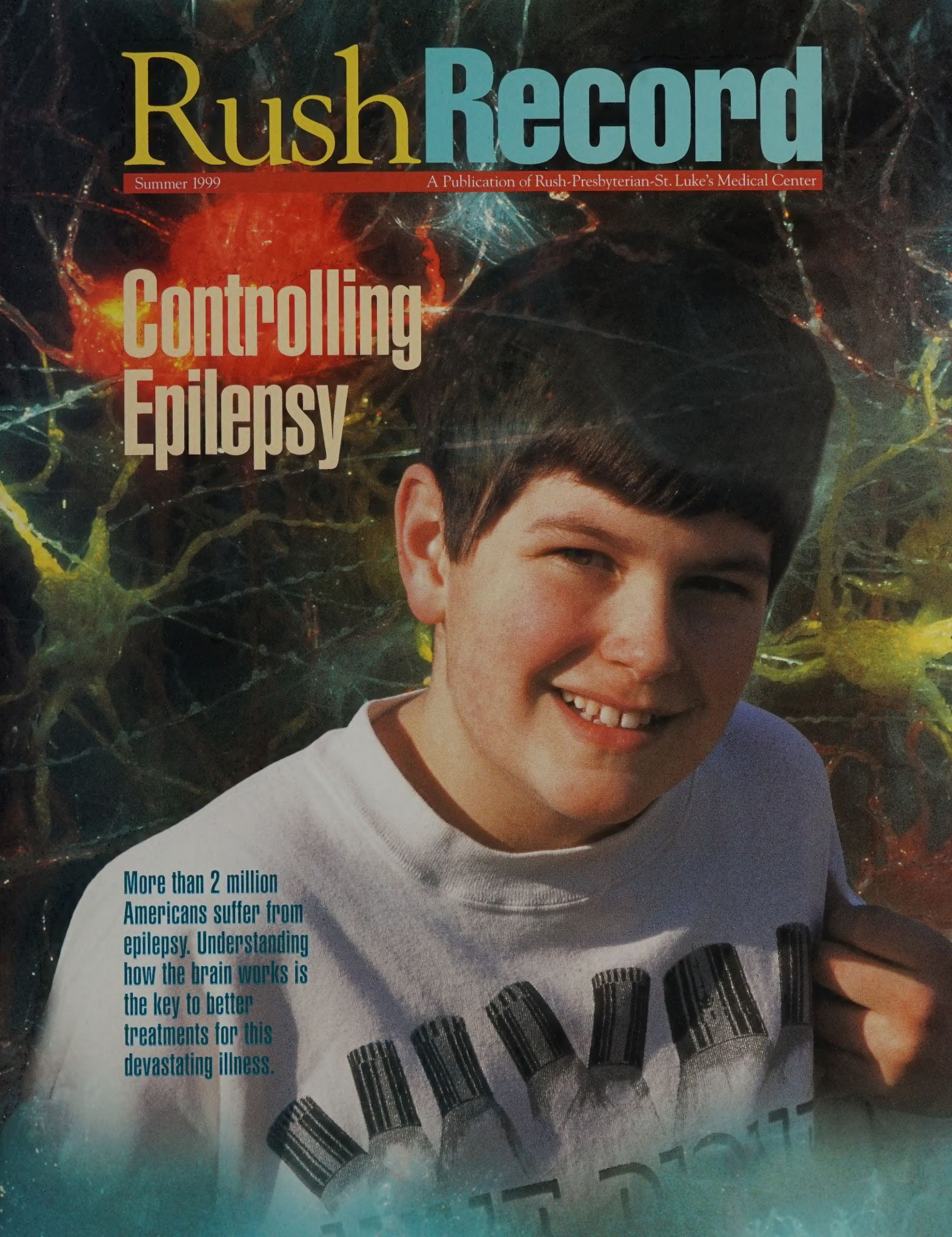
Rush Record
Summer 1999
A Publication of Rush-Presbyterian-St. Luke's Medical Center

Controlling Epilepsy



More than 2 million Americans suffer from epilepsy. Understanding how the brain works is the key to better treatments for this devastating illness.

RushRecord
Summer 1999

Editor:
Marie Mahoney

Managing Editor:
Jill Waite

Writers:
Charles Bila
Sean Carr
Judy Grossman
Aaron O. Hall
Anne M. O'Reilly
Laura Ramos
Lisa Spengler

Design and Art Direction:
Brierton Design

RushRecord is a publication of Rush-Presbyterian-St. Luke's Medical Center, produced by the Office of Philanthropy and Communication.

Jack R. Bohlen
Vice President

Diane McKeever
Associate Vice President

Ellen M. Hunt
Director of Publications

Rush-Presbyterian-St. Luke's Medical Center
1700 West Van Buren, Suite 250
Chicago, IL 60612

For additional information on any of the articles in this issue, please call (312) 942-5580.

A Member of the
Rush System for Health

RUSH

Contents

6

Understanding epilepsy helps doctors and researchers explore new treatments.

2

Doctors move beyond the mainstays of rest and muscle relaxants to fight lower back pain.

12

In the Philippines, surgical teams help children with cleft lips and palates find their smiles.

15

Researchers envision a day when people in desperate need of organ transplants won't have to wait.

28

Hillary Clinton visits Rush.

Cover Story

Controlling Epilepsy
Advanced treatment options help adults and children with epilepsy lead normal lives — *by Anne M. O'Reilly* 6

Features

Back in the Swing
Rush physicians explore new ways to alleviate back pain — *by Charles Bila* 2

A Thing of Beauty
Rush doctors and nurses travel abroad to treat children with facial deformities — *by Laura Ramos* 12

Crossing Barriers
Researchers explore the possibility of using animal-to-human organ transplants — *by Lisa Spengler* 15

A Life of Extremes
Treatment guidelines help victims of bipolar disorder find balance — *by Marie Mahoney* 18

Medicine's Super Sleuths
Behind the scenes, pathologists solve medical mysteries — *by Jill Waite* 22

Rush Rounds

The virtual classroom • Korean nurses visit Rush • Jacobs named to Crown chair • Rush's comparative research program accredited • Brennan takes reins as Trustees chair • Trott elected general trustee • Medical Center names new department chairs 24

Medical Fronts

Staying the course: Rush researcher helps heart patients follow doctors' orders • Rush physician lead author of stroke prevention guidelines • New treatment may be alternative to chemotherapy for non-Hodgkin's lymphoma • Bioartificial liver sustains patient awaiting transplant 26

One Last Thought

First Lady Hails Rush Epilepsy Center 28

George Lofton hits the links after spine surgery at Rush.

Photos by Andrew Campbell

Back in the Swing

by Charles Bila

After the common cold, back pain is the second most frequent complaint heard in doctors' offices. It is also the most common reason for disability, and costs more than $27 billion in lost productivity each year. Knowledge gained from research on the causes of back pain is helping physicians craft new approaches to diagnosing and treating the problem.

Back pain wasn't the kind of handicap George Lofton wanted in his golf game. But one morning after hitting the links, he woke up with excruciating pain in his lower back. He could barely walk. His wife rushed him to the emergency room of a hospital near their South Side home. For a while, Lofton, a 52-year-old director of economic development for Commonwealth Edison Co., thought his active life and career had come to an end.

But Lofton didn't have to put his golf clubs in storage. He is one of many patients who have benefited from a refined understanding of the intricate architecture of the human spine. This knowledge has led to improved surgical techniques and to new recommendations regarding treatment, allowing physicians who treat back pain to move beyond the old mainstays of rest and muscle relaxants.

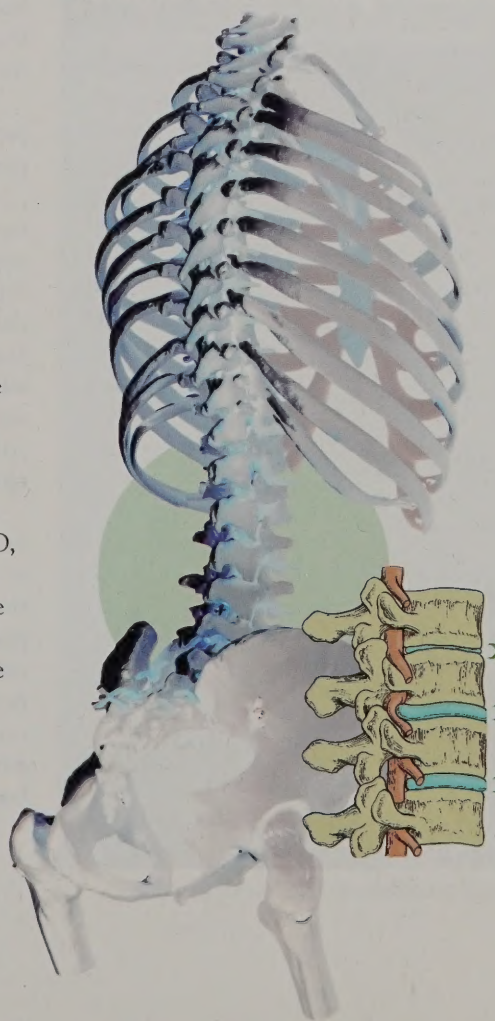
"Take two aspirin and *don't* call me in the morning was the case a few years ago," says Gunnar Andersson, MD, PhD, chair of the Department of Orthopedic Surgery at Rush. "Today, however, more and more patients are referred to me at the appropriate time for the appropriate reasons. There is a better awareness among doctors in general about back pain and how to deal with it."

Choosing the right course

A week after his emergency room visit, Lofton was back on the golf course. He limped slightly and had occasional back spasms but nothing he couldn't live with.

But a few days later, Lofton noticed that his right leg was weaker than his left. He consulted orthopedic surgeon Mitchell Sheinkop, MD, a hip and knee specialist at Rush. Sheinkop noted some muscle loss in Lofton's calf, but an MRI of Lofton's leg was normal. An MRI of his back, though, found a slipped, or herniated, disc. Vertebral discs, made of tough but flexible cartilage, cushion the vertebrae and enable the spine to move smoothly. In Lofton's case, the slipped disc was pressing against his sciatic nerve, a nerve that extends from the pelvis to the backs of the knees. As a result of the pressure, Lofton developed sciatica, severe pain that radiates from the lower back down to the legs.

Sheinkop referred Lofton to Howard S. An, MD, the Morton International Professor of Orthopaedic Surgery at Rush. An, who specializes in spinal surgery, told Lofton that his back problem was mostly neurological — that is, due to nerve weakness or damage. Consequently, An thought conservative treatment, such as medication combined with a gradual return to normal activities, would probably be effective. But he also cautioned that untreated nerve deficits can sometimes become permanent.



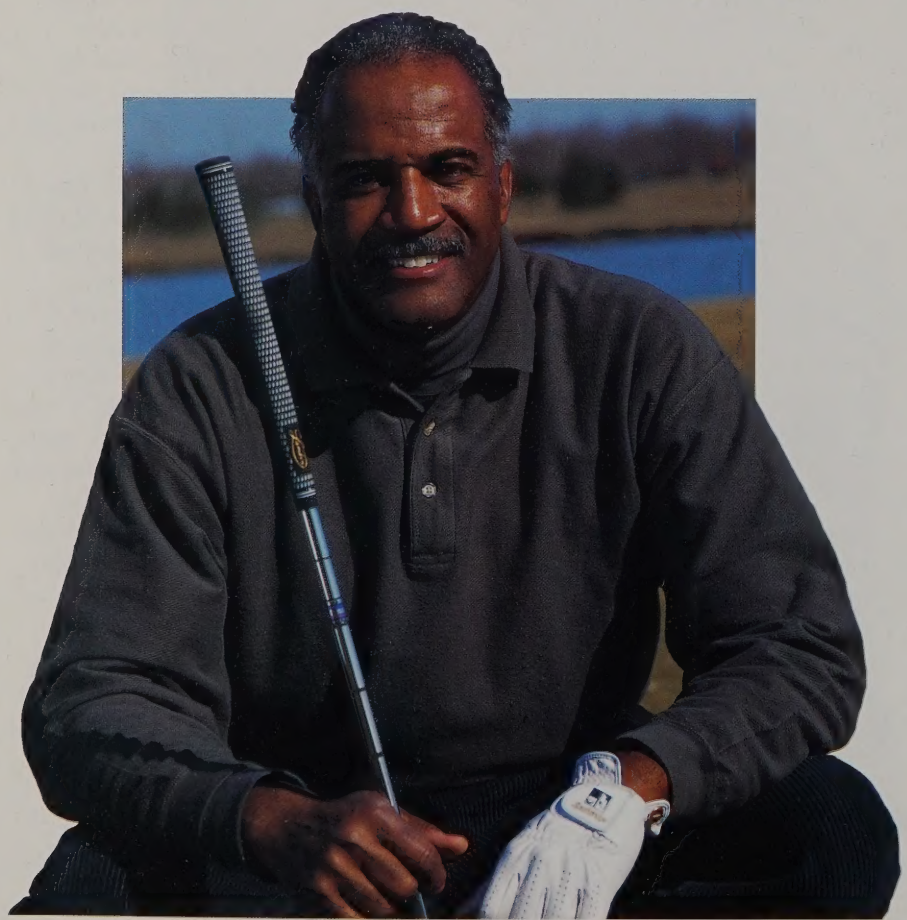
A refined understanding of the intricate architecture of the human spine has led to improved surgical techniques and to new recommendations regarding treatment. This has allowed physicians who treat back pain to move beyond the old mainstays of rest and muscle relaxants.

"Only 15 to 20 percent of herniated disc cases require surgery," An says. "A lot of patients choose to live with mild leg weakness or numbness. But in patients who are very active, like Lofton, weakness is not acceptable."

In Lofton's case, An recommended a surgical procedure called a limited approach discectomy. This technique, which takes advantage of sophisticated microsurgical instruments, allows surgeons to remove the herniated disc through a small incision in the lower back. Because the procedure is less invasive than traditional surgery, patients recover and can get back to their regular activities sooner.

Before Lofton made a treatment decision, he did some research on back surgery, got a second opinion and interviewed other patients with back pain. "I talked with a lot of people trying to live with low back pain," he says. "It was at that time that I knew what I had to do."

In October of 1998, two months after his injury on the golf course, Lofton was admitted to Rush for the operation. He went home the same day and was back on his feet and walking two days after that. After his sixth and final physical therapy session in June, Lofton expects to function at 100 percent — the only remnant of his surgery being a one-inch scar below his swimming trunk line. He may never have a single digit handicap in golf, but he should be able to finish an 18-hole course.



George Lofton took advantage of a new microsurgical procedure to repair a slipped disc.

Understanding the back

As people age, avoiding back injuries becomes more difficult. By the time most people reach the age of 40, tiny cracks and fissures in vertebral discs are the rule, not the exception.

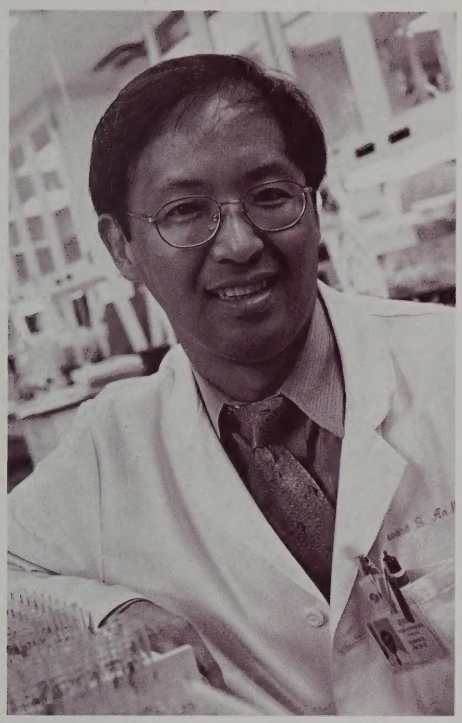
"Every fifth adult in this country will have back pain in a given year," Andersson says. "Most of the time, these episodes are short-lived and benign. They go away in a week or two with conservative treatment and are a temporary disorder for the patient."

According to Andersson, more than 90 percent of the cases of acute back pain — or pain that lasts no more than six weeks — can be treated nonsurgically.

The situation is more complicated for patients who suffer from chronic back pain, which can last for years or a lifetime.

"With chronic pain, the central nervous system is affected, and the pain needs to be dealt with as an entity," Andersson says. "Doctors also have to deal with the social factors surrounding the patient." Patients who are overweight or who smoke — which accelerates the aging process — have a higher risk of developing both acute and chronic back pain.

The good news is that increasing numbers of patients who don't respond to conservative treatment — whether they suffer from chronic or acute back pain — can benefit from surgery. Diagnostic tests like MRI scanning that have been perfected over the past two decades, improved surgical techniques and new research findings on the causes of back pain have all combined to make



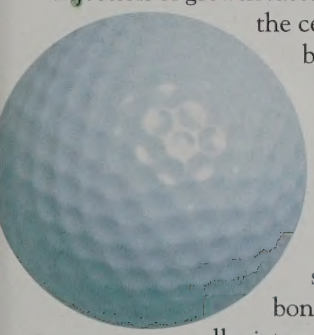
Howard S. An, MD

surgery a more attractive treatment option today than it was 20 years ago.

Designing new treatments

To further refine treatments, physicians and scientists at medical centers like Rush are conducting studies on how damage from back injuries, as well as the normal wear and tear of aging, cause back pain. They are also exploring ways to use natural substances to repair damaged tissue.

"We have been examining how the injection of growth factors can replenish the cellular matrix in back tissue," An says. A traditional approach in back surgery involves fusing damaged spinal discs with bone. This helps alleviate pain, but also restricts movement. As a result, recovery is sometimes limited, An says. "With injection, the patient may have a better recovery rate, while preserving motion, without the need for surgery."



Some people have back pain as a result of biochemical changes in the cushioning cartilage that makes up the vertebral discs. Back pain results when this cartilage loses its ability to function as a shock absorber. An and his staff are conducting research on how natural growth factors — proteins that stimulate tissue growth — may restore disc tissues.

In other studies, Rush scientists are investigating how tissues in the back — muscles, cartilage and bone — react to injury or physical stress. These clinical trials, An says, will help physicians understand how these biomechanical changes can affect a person's range of movement.

These studies have helped physicians craft nonsurgical treatments as well as safer surgeries. But the ultimate goal is to keep problems from developing in the first place, An says. "Understanding more about the biomechanical and biochemical functions of the back is not only important to understanding how to treat back pain but how to prevent it as well." ■

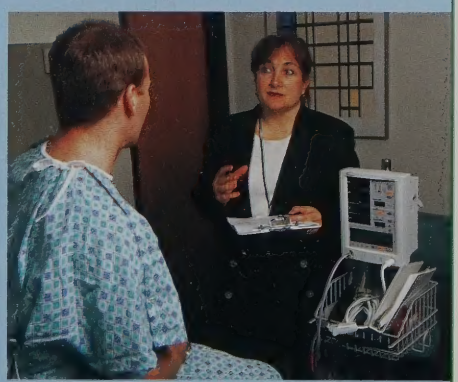
Center offers comprehensive care for the spine

Rush has launched a new program offering coordinated services — including diagnosis, medical care and rehabilitation — for patients with neck and back problems. The Rush Spine Center is housed at Oak Park Hospital, a member of the Rush System for Health located in Chicago's Near West suburbs.

Health care institutions across the country are establishing such multidisciplinary centers, says Bonnie Clipper-Salzberg, MA, MBA, RN, vice president of patient care services at Oak Park Hospital. Orthopedic surgeon Howard S. An, MD, is the center's medical director.

The center's staff includes orthopedic surgeons, neurosurgeons and physiatrists, the physicians who specialize in physical therapy and rehabilitation. The center will eventually integrate complementary services, such as acupuncture and chiropractic care, according to Clipper-Salzberg.

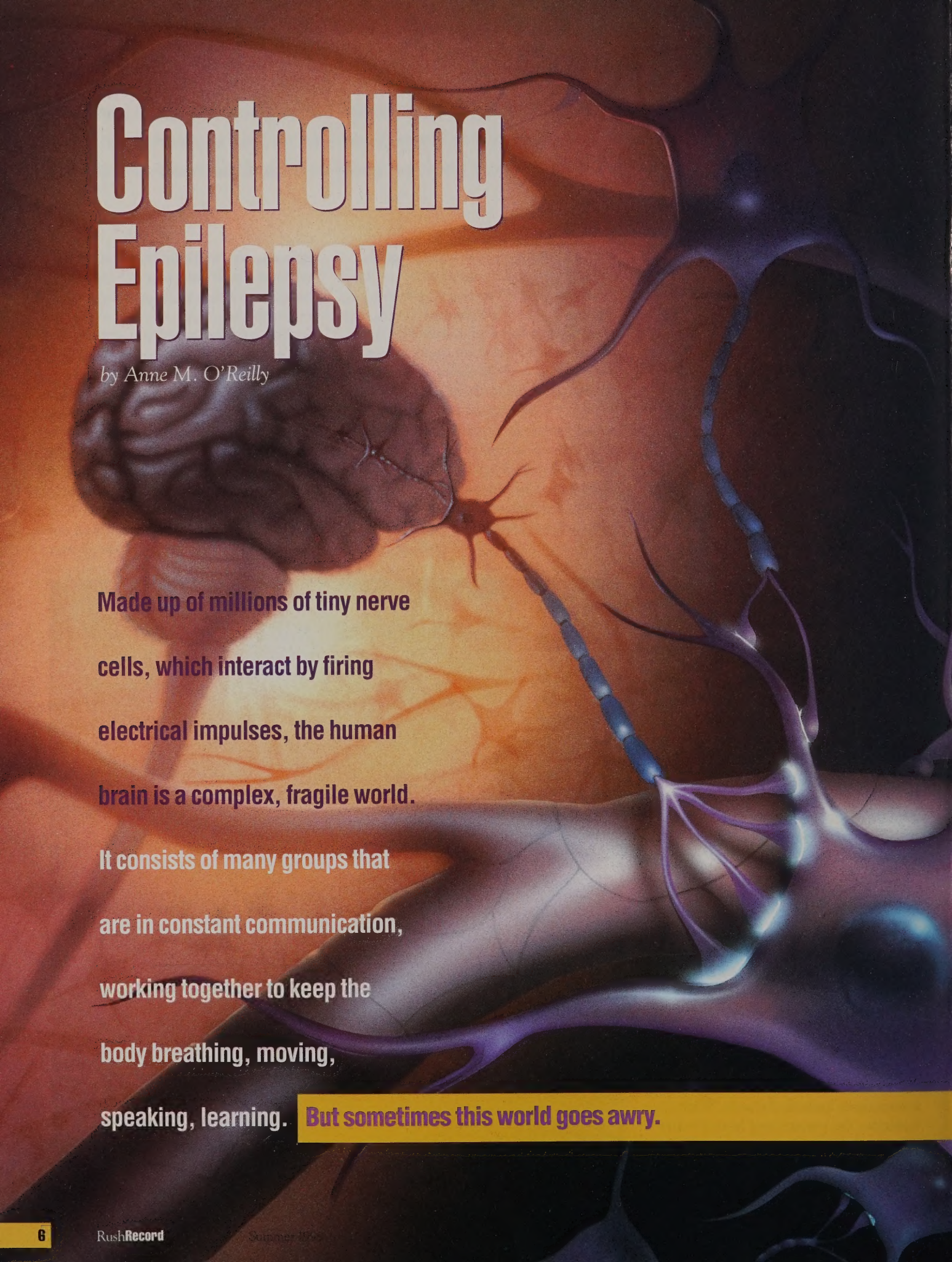
"I think we'll get to a point in treating spine problems where we will be offering neither traditional therapy nor alternative therapy," she says. "Instead, we will integrate the best of traditional and complementary approaches. Our hope is that this will ultimately equate to better patient care."



The Rush Spine Center at Oak Park Hospital offers multidisciplinary care for patients with neck and back problems.

Controlling Epilepsy

by Anne M. O'Reilly



Made up of millions of tiny nerve cells, which interact by firing electrical impulses, the human brain is a complex, fragile world. It consists of many groups that are in constant communication, working together to keep the body breathing, moving, speaking, learning. But sometimes this world goes awry.

A tumor, genetic problem, infection, gunshot wound or blow to the head may cause more damage than the immediate injury itself would suggest. Any of these insults to the brain can prompt the same destructive result: millions of these nerve cells, or neurons, misfiring in a synchronized pattern, causing epileptic seizures. If these seizures persist, they can alter brain functions for a lifetime.

An estimated 2.3 million Americans suffer from epilepsy. About 75 percent find medications or other treatments that control their seizures. The other 25 percent try everything available to alleviate their seizures and find no relief. They suffer from intractable, or uncontrolled, epilepsy. An adult with uncontrolled epilepsy may not be able to hold a job, drive a car or maintain personal relationships. If their seizures are violent, patients risk serious injuries or even death. For children, whose brains are developing, the results of epilepsy can be especially devastating, often interfering with learning and other cognitive functions during critical stages of growth.

"The problem of medically intractable epilepsy is significant, because the more seizures you have, the more seizures you'll get," says Michael Smith, MD, director of the Rush Epilepsy Center.

Many patients with uncontrolled epilepsy seek help at the Rush Epilepsy Center, which offers advanced treatment options and research capabilities not widely available.

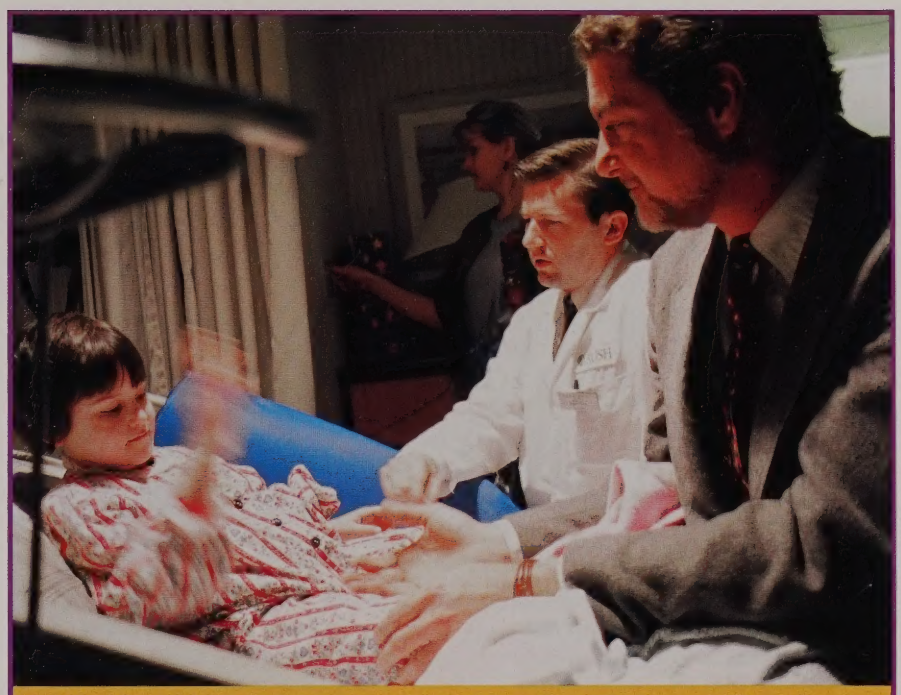


Photo: Andrew Campbell

Michael Smith, MD (right), and neurology fellow Kurt Washburn, MD, with a young patient at the Rush Epilepsy Center.

What is a seizure?

Treatment of epilepsy depends on understanding a patient's seizures, which fall into two broad classifications — generalized and partial. The type of seizure depends mainly on where in the brain the epileptic activity starts and on the direction and speed of its spread.

Generalized seizures affect the whole brain and alter consciousness. Partial seizures affect part of the brain and take two forms: complex partial, in which the patient loses consciousness and has no memory of the event, and simple partial, in which the patient is conscious and aware of what is happening.

Although the word seizure often brings to mind violent convulsions, many people with epilepsy don't experience convulsions at all. Some seizures involve repetitive movements of the hands and face, such as smacking or licking of the lips, picking at clothing and repeated hand movements.

When Sharon Datro, 46, began having seizures in 1979, her friends and family didn't notice at first. "I was known as the person who really didn't pay attention and liked to pick at my clothes," says Datro, who was having about seven or eight seizures a month. Because she had complex partial seizures, she had no memory of them.

Datro would have remained oblivious of her seizures if it hadn't been for the day she had one while bowling. "I dropped a bowling ball on my foot, and I didn't remember," she says. After a visit to her doctor, Datro was diagnosed with epilepsy.

Phil and Jill Gattone's son, Philip Jr., was diagnosed with intractable epilepsy in April of 1991, when he was 4 years old. After visits with specialists around the country, the family's search for help led them to Rush in 1992.

Philip's epilepsy began with generalized tonic-clonic seizures, formerly known as grand mal seizures. Tonic-clonic seizures are characterized by violent stiffening of the body and convulsions.

Eventually, Philip's epilepsy manifested itself in different ways, as more areas of his brain "learned" to have seizures. He experienced complex partial seizures. Then he began having what physicians refer to as generalized absence seizures, characterized by

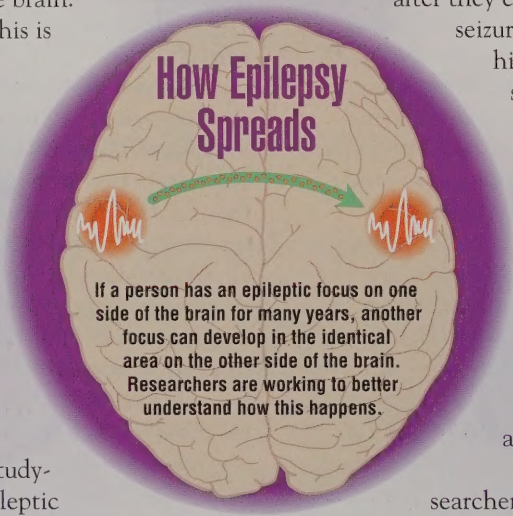
For children, whose brains are developing, the results of epilepsy can be especially devastating.

Epilepsy research seeks new and better treatments

Early in 1990, then-president George W. Bush declared the beginning of the Decade of the Brain. As the decade comes to a close, neuroscientists continue to seek new knowledge about the intricate workings of the human brain. Researchers at the Rush Epilepsy Center are helping to lead the way through studies of the causes of epilepsy and its treatment.

Some of that research is based on the work of former epilepsy center director Frank Morrell, MD, who died in 1996. In addition to pioneering new treatments for the disease, Morrell developed a theory to explain how epilepsy spreads from one side of the brain to the other — a process called secondary epileptogenesis. Following initial studies in animals, Morrell discovered that if a person has an epileptic focus on one side of the brain for many years, another focus can develop in the identical area on the other side of the brain.

Although this is somewhat rare overall, it happens nearly 40 percent of the time in epilepsy cases caused by brain tumors, says neuroscientist Leyla deToledo-Morrell, PhD. She and her colleagues are studying how the epileptic focus spreads from one side of the brain to the other. "Using animal models, we'll be examining factors that cause the spread," deToledo-Morrell says. "My husband demonstrated that the important factor is not electrical activity. Some molecule seems to be transported from one side of the brain to the other, but we don't yet know the nature of what is transported."


How Epilepsy Spreads
If a person has an epileptic focus on one side of the brain for many years, another focus can develop in the identical area on the other side of the brain. Researchers are working to better understand how this happens.

In other research, neuroscientist Thomas Hoeppner, PhD, and Michael Smith, MD, director of the epilepsy center at Rush, are studying how the brain learns to have seizures. They also are analyzing the spread and intensity of seizures and new medications to block the growth of seizures.

"So far, we have seen evidence that portions of the brain that are involved in epilepsy and seizures also have disturbed functions between seizures," Hoeppner says. "We've seen evidence that early treatment can improve function between seizures."

Rush doctors and researchers are concerned not only about stopping seizures, but also about patients' quality of life. Rush researchers believe there is a link between depression and epilepsy. In a recent study, Andres Kanner, MD, found that 50 percent of people with epilepsy became depressed for about 36 hours after they experienced a seizure. Kanner and his colleagues are studying the neurochemical changes that accompany seizures in an effort to understand why depression often results and to create appropriate treatments.

As Rush researchers continue to work toward a cure for epilepsy, Smith says controlling some seizures is not enough. "The goal of epilepsy therapy is to achieve a seizure-free state without side effects," he says. "We should treat epilepsy like heart problems. You can't be a heart patient who still has heart attacks. We need to aggressively treat seizures when they first occur."

eye-blinking, head-bobbing and a glazed expression.

The seizures were taking a toll on the young boy's development, says his mother. "By the fall of 1993, Philip's seizures were out of control," she says. "He was having 10-second blinking spells every two to three minutes. Philip was not speaking fluently. It would take him two minutes to say, 'I want to go outside and play.'"

Like every patient who visits the Rush Epilepsy Center, Philip Gattone and Sharon Datro went through various tests to diagnose the condition and to discover the right way to treat their particular forms of the disease.

The brain at work

Because seizures provide clues about what is going wrong in the brain, watching seizures take place is essential to diagnosis. The six-room Rush Epilepsy Monitoring Unit allows doctors to observe patients having seizures inside a safe, controlled environment.

Patients are videotaped 24 hours a day so that all seizures are detected, even those that occur while the patient is sleeping. The videotapes help to identify the type of epilepsy, recording certain symptoms such as the patient's facial expressions or abnormal or unusual behavior.

To help determine the type of seizures a patient is having, and therefore the best course of treatment, patients also undergo electroencephalographic (EEG) monitoring, which measures electrical activity throughout the brain.

Doctors examine the EEG reading for any abnormalities in brain activity. With the EEG, doctors sometimes can pinpoint the epileptic focus, or where the epileptic activity is located in the brain.

Because patients suffer memory impairment during some types of seizures, they are interviewed and examined immediately after seizures. Technicians make note of any changes in behavior or memory.

Rush is one of the few hospitals in the nation with such a unit. The monitoring unit is dedicated to the epilepsy center's former director Frank Morrell,

MD, an internationally recognized physician and scientist who died in 1996.

Before he died, Morrell worked closely with his wife, Leyla deToledo-Morrell, PhD, on a new protocol using Magnetic Resonance Imaging to identify the location of the epileptic focus in patients whose seizures originate in the brain's temporal lobe, an area of the brain that plays a crucial role in memory. An MRI, used in coordination with an EEG, is another noninvasive way to discover where seizures are coming from, deToledo-Morrell says.

MRI scans are taken of a patient's brain, then transferred electronically to a computer program. Using sophisticated imaging capabilities, the program allows researchers to view the brain scan as a three-dimensional ball. Then, further "cuts" can be made to get a closer look, deep inside the brain.

Identifying as precisely as possible the focus of epileptic activity is crucial, especially when surgery is being considered. "Surgery is an option only when you know the site of origin," says Thomas Hoeppner, PhD, a Rush neuroscientist. "If you can stop epileptic activity at the original site, you can stop the spread."

Neuropsychology, or the study of brain behavior, also plays a role in diagnosis and in identifying which patients may benefit from surgery. Christopher Grote, PhD, tests patients' memory, concentration and other areas of cognitive ability. These tests are helpful in determining which parts of the brain are involved in seizures and in reducing the risk of problems with memory or speech after surgery.

Photo: Andrew Campbell

Mission control for the Rush Epilepsy Monitoring Unit, which enables around-the-clock observation of patients.

Getting seizures under control

Once patients are diagnosed accurately, controlling seizures is the goal. For many people with epilepsy, medications are effective.

Within the last 10 years, several drugs have been introduced that greatly benefit people who suffer from epilepsy. "We have more than doubled what was previously available," says neurologist Donna Bergen, MD. Rush has been involved in many experimental drug studies since Morrell established the epilepsy center in 1972.

Most of today's epilepsy drugs act as anticonvulsants. Rather than stopping seizures at the source, the medications halt the spread of the activity in the brain.

Another relatively new option to control seizures is a pacemaker-type device that connects to the vagus nerve in the neck. The vagus nerve is one of a group of nerves, known as the cranial nerves, that originate in the brain and are involved in regulating crucial bodily activities like breathing, heart function and digestion. This device, smaller than the palm of a hand, is implanted beneath the skin in the chest. It is linked to the vagus nerve and sends out tiny electrical impulses to stimulate the nerve. The nerve then carries the impulses to the brain, where they reduce or stop seizures. Patients typically use the vagus nerve stimulator in combination with at least one medication.

The results of using the vagus nerve stimulator are comparable to those of medications. The number of seizures is reduced by more than 50 percent in about 30 to 40 percent of patients, says neurologist Ruzica Ristanovic, MD, who was one of the first physicians to test the device in Chicago-area clinical trials. Many neurologists believe the vagus nerve stimulator is the first step toward the creation of a device that will be

Within the last 10 years, several new anti-epilepsy drugs have been introduced. "We have more than doubled what was previously available," says neurologist Donna Bergen, MD.

permanently implanted in the brain to prevent seizures.

The vagus nerve stimulator also offers help to some patients who are frustrated with the side effects of medications. Patients often complain that epilepsy drugs dull their senses and cause confusion and fatigue that significantly alter their daily lives, Smith says. Many patients with intractable epilepsy take multiple medications, which may interact and cause further cognitive problems, Ristanovic says. With the vagus nerve stimulator, the patient does not suffer from complications due to drug interactions, she adds.

Epilepsy surgery

Many patients who are not helped by the vagus nerve stimulator and who find their medication regimens intolerable and insufficient to stop their seizures ultimately turn to surgery.

Photo: Andrew Campbell

Rush patient Sharon Datro, on the job in the City of Chicago's Legal Department.

That was the case for Datro. At one time, she was taking about 25 pills a day. But her medications were not eliminating her seizures, and she often felt extremely tired.

"I could never walk heel to toe, and I usually looked a little off balance to other people," says Datro, who works as a receptionist in the City of Chicago Legal Department. "I would walk to the bus stop in the morning and sometimes I would pretend that my leg hurt to keep my balance. I was even accused of being drunk sometimes."

Since the late 1980s, the number of medical centers providing surgical therapy for epilepsy has nearly doubled. Certain types of epilepsy, particularly epilepsy involving the temporal lobe, can be treated surgically and cured in 60 to 80 percent of patients, says Rush neurosurgeon Richard Byrne, MD.

That surgical procedure usually means removing malfunctioning brain cells, as was the case for Datro. In 1996, she had a right temporal lobectomy, in which epilepsy-causing tissue was removed. This is the most common surgery done at the Rush Epilepsy Center.

Her surgery was an overwhelming success. Datro, who has been seizure-free for nearly three years, says that her life has changed dramatically since her surgery. "I enjoy life so much more," she says. "I just enjoy walking and talking to people. I'm so happy all the time now."

She credits Smith with her success. "I saw many doctors before I found Dr. Smith, but this is where I found a cure," she says. "With all of his hard work, he shows his patients how much he cares."

In an effort to cut down on long-term complications of epilepsy surgery, Rush tailors surgeries specifically to the epileptic focus in the patient's brain. This way, as little brain tissue as possible is removed, potentially reducing the incidence of memory problems or the loss of certain skills patients had before the surgery, says Rush neurologist Andres Kanner, MD. Kanner is researching the long-term results for patients who have tailored resections compared with standard resections. Preliminary results suggest that the tailored resections have less risk of long-term complications for the patients.

Photo: Jean Clough

Implanted in the chest, the vagus nerve stimulator can help reduce or stop seizures.

A different world

Like Datro, Philip Gattone also sought relief through surgery. His medications were not alleviating his seizures, and the young boy was losing precious time for development. Because of the toll the seizures were taking on his brain, his IQ dropped from 115 to 72 in less than two years.

"At 6 years old, he started to lose a lot of his cognitive abilities," his father, Phil Sr., says. "We knew we had to do

Certain types of epilepsy, particularly epilepsy involving the temporal lobe, can be treated surgically and cured in 60 to 80 percent of patients.

something." With Smith's advice, the Gattones chose surgery to control their son's problems.

In 1993, the boy underwent a surgical procedure called multiple subpial transection, a treatment advance pioneered by Morrell and Walter Whisler, MD, PhD, former chairman of the Department of Neurosurgery. The surgery was designed to help those who have epileptic activity centered in the areas of the brain critical to speech, movement and sensation. The procedure is based on the fact that the brain is organized into columns, in which the most important connections for function are vertically oriented. Multiple subpial transection allows horizontal fibers to be cut to prevent the spread of seizures, without affecting other important brain functions.

After a second surgery, a temporal lobectomy in 1994, the results for young Phil were just as good as Datro's. He has been seizure-free for the last five years.

Philip, now 12, is like any other boy his age. He likes to spend time playing with his brothers, Mike, 9, and John, 8, as well as his sister, Becky, 5. The dark-haired, bright-eyed boy enjoys football and white-water rafting.

The Gattones are thrilled to see their son doing so well. "This is what happens when research, dedication and commitment come together," says Philip's father, who says of his son, "He is our hero." ■

Educating the public about epilepsy

When Phil and Jill Gattone's son, Philip Jr., was in second grade in 1994, he was having trouble in school. His frequent seizures because of epilepsy were taking a toll on his ability to learn and on his relationships with other children.

"The other kids were isolating him," his father says. "They didn't understand what was going on. He was writing maybe a sentence or two while they were writing a whole page. He knew that and they knew that. And his behavior wasn't like theirs because of the medications he was taking."

To help the kids understand what Philip Jr. was going through, his parents visited their son's class. "The kids were fantastic," Phil says. "They were asking questions, relating their experiences to his. They started to connect with Philip, and that had a huge effect on him."

Based on the experience of talking to Philip's classmates, the Gattones started the Center for Epilepsy Education, an organization dedicated to promoting public awareness of the challenges facing children and adults with epilepsy.

Now Phil Gattone, whose son no longer has seizures after two surgeries at Rush, is running the Rush Epilepsy Education and Outreach Initiative with Janice Buelow, MS, RN. "I'm fortunate that I'm able to work in the place that saved my son's life," he says.

Gattone visits schools, organizations and companies to talk about the stigma often associated with epilepsy. Michael Smith, MD, director of the Rush Epilepsy Center, says people who have the disease are often faced with discrimination.

"No matter how alike we think we are, if one of us had a grand mal seizure, we would treat that person differently," Smith says. "When something scares you and you don't understand it, you discriminate against it. That's one of the biggest problems for our patients with epilepsy."

Social worker Silvana Chavez, LSW, also helps Rush epilepsy patients cope with the many day-to-day problems associated with the disease. She counsels patients and puts them in touch with organizations and services. "They're feeling like doors are closing," she says. "Some find that all of a sudden they're unemployed. As their life changes with the illness, I'm here to help them open different doors."

To help prevent discrimination at work or in school, Gattone provides employers and teachers with accurate information about the disease.

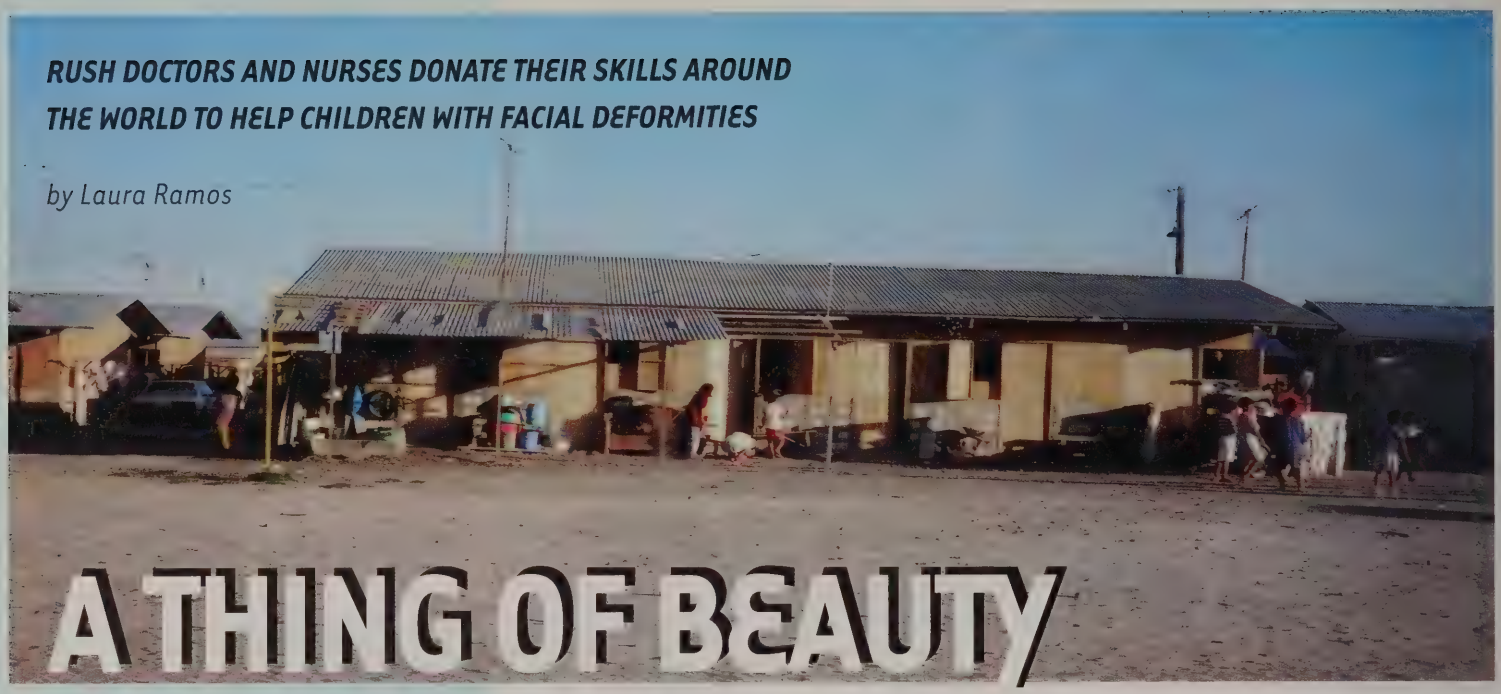
"When your child has epilepsy, it has a dramatic effect on the whole family, on brothers and sisters, on a marriage, on work — its effects are profound," he says. "This is what families are dealing with every day. So to have another battle with the school or your employer, it becomes overwhelming. We offer not just advocacy, but real, practical solutions."

Rush patient Philip Gattone, Jr., with his parents, Phil Sr. and Jill.

Photo: Andrew Campbell

RUSH DOCTORS AND NURSES DONATE THEIR SKILLS AROUND THE WORLD TO HELP CHILDREN WITH FACIAL DEFORMITIES

by Laura Ramos



A THING OF BEAUTY

From left to right: The remote Mabalacat District hospital; Schafer and crew take a momentary break in the madness for a smile; volunteers relax after a hard day's work.

Rush plastic surgeons have heard "thank you" spoken a lot of ways: "gracias" in Spanish, "kob koon" in Thai, "shukriya" in Hindi and "salamat po" in Tagalog, the predominant language of the Philippines. That's because each year, these doctors travel halfway around the world to change the lives of children born with facial deformities.

But perhaps the kindest thanks they receive is when a child smiles without shame for the first time. It's these moments that make Rush plastic surgeons Craig Bradley, MD, and Michael Schafer, MD, give two weeks of their time each year to travel to faraway places to carry out their work.

A journey to the other side of the world: The Philippines

This spring, Rush plastic surgeon Michael Schafer, MD, returned with 15 doctors and nurses to the Philippines, a country where thousands of children are born with cleft lips and palates every year. An Asian nation of 7,100 separate islands stretching 1,100 miles north to south, the Philippines has a rural population affected by poverty, lack of sufficient medical care and poor nutrition.

"Children who do not have a timely repair of their cleft lips and palates frequently become self-conscious, do not go to school and become social outcasts," Schafer says.

Initially, Schafer's missions were funded in part by the Foundation for Children's Reconstructive Surgery, an organization started by Schafer, Bradley and another Chicago plastic surgeon, Robert Swartz, MD. Funding has also been made available through the Clarence Monroe Fund at Rush. This fund honors Clarence Monroe, MD, a plastic surgeon who volunteered his services overseas and served on the medical staff at Presbyterian-St. Luke's Hospital for 41 years until his retirement in 1974. Recently, Schafer's missions have been supported by Operation Rainbow, a Houston-based surgical mission foundation.

In March, Schafer embarked on his 13th trip to the Philippines, where he was joined by 15 other doctors, nurses and volunteers.

The doctors and nurses work in hospitals in the Philippines to provide free surgery to patients for whom it would otherwise be either unavailable or unaffordable. The team relies on contact people in the Philippines to be their agents. These local contacts arrange times and places, help promote the free surgeries through various news media and arrange for patients to be admitted to hospitals for the surgeries.

This year, a group was invited to the Rogadacio Mercado Memorial Hospital in Bulacan Province, about one hour north of Manila, where they treated 55 patients, performing about 70 surgeries during five days of work.

"The patients coming for this care are usually indigent, and many travel great distances, so the follow-up is sometimes more difficult than we would like," Schafer says. "One patient's mother travels three days by boat to thank us for our work each time we visit."

"THE TEAM'S ABILITY TO IMPROVISE IS CRITICAL TO ITS SUCCESS. I LIKEN IT TO A COMBINATION OF M*A*S*H AND 'CIRQUE DE SOLEIL.'" — MICHAEL SCHAFER, MD

One tough vacation

Performing surgery in Third World countries often means working under conditions quite different from those at home, Schafer says. The medical staff often works with only a minimum of the sophisticated instruments and modern equipment to which they have become accustomed. Certain "creature comforts" — like telephones and air conditioning — are sometimes lacking. It isn't uncommon to encounter the absence of toilet seats and for the electricity to fail in the middle of an operation.

"We've done a lot of work by flashlight," Schafer says, adding, "The team's ability to improvise is critical to its success. I liken it to a combination of M*A*S*H and 'Cirque de Soleil.' We set up very quickly, we are very efficient, we improvise well and we function with amazing precision."

The workdays are long, starting at 7 a.m. and often continuing late into the evening. By the time the team arrives at the hospital each morning, the children and families are lined up outside waiting their turns.

Treating patients under the conditions of foreign medical missions requires special care and attention to detail. "Many of the children who come to us have underlying medical problems, in particular malnutrition, extensive dental pathology and respiratory illnesses," says Caroline Kunz, RN, who has been the operating room team leader on six recent missions to the Philippines. She explains that poverty and somewhat primitive living conditions contribute to these medical conditions.

Kunz says she is always impressed by the bravery of the children having surgery. "They are very stoic," she says. "They seldom cry. They seem to take comfort from being in the hospital with other children who have similar problems. And they seem to know that they are being made to look like other children."

The surgical team always includes native-speaking people to facilitate communication with patients, family and staff at the host hospitals. Belle Pecson, RN, a nurse coordinator in the post-anesthesia recovery unit at Rush, has been the recovery coordinator and a principal translator for the last six Philippine mission trips.

Pecson is often the first person to see the children as they wake up after their surgery. She is able to console them in their own language, and helps lessen their fears. "Their first reaction is almost always a mixture of fear and delight," she says. "We help them awaken from anesthesia, then we give them a mirror to look at. Often children turn to their parents and say, 'Look how beautiful I am!'"

Staying hooked

With a 21-hour plane trip, 16-hour workdays and 100-degree heat, a mission trip to the Philippines is hardly a cushy vacation. But most volunteers keep going back. "Everybody comes back grateful for what we have and for the opportunity to share what we have with others who are less fortunate," Schafer says.

Schafer now plans to extend the scope of his mission work. He and a small team have recently returned from a site visit to an academic medical institution in Ha Noi, Viet Nam. Plans are under way to develop cooperative programs — including clinical work, lectures and exchange programs — between the medical school in Viet Nam and Rush Medical College.

Passage to India: A labor of love

India is home to some of the best doctors in the world. Still, it doesn't have enough plastic surgeons to care for the masses of poor people who crowd its public hospitals. And what a crowd it is. India has roughly one-third the land mass of the United States, yet its population is nearly three times as large.

"There are major demands on the public hospitals in India, which look like American hospitals around 1950," explains Rush plastic surgeon Craig Bradley, MD, who has led or participated in several surgical missions to developing countries over the last 15 years. "They have limited resources, and often sterilize and reuse the things we throw away, like suture remnants and sterile sheets."

To help alleviate some of the burden on India's doctors, Bradley was invited by Indian medical professionals to a hospital in Coimbatore in southern India. February marked Bradley's first mission to India to mend some of the population's cleft lip and palate problems. The mission was supported by the Rush Woman's Board.

While in India, Bradley was joined by a team of physicians, nurses and several volunteers. Members of the team included anesthesiologist Scott Pitman, MD, from Rush North Shore Medical Center in Skokie; nurse anesthetist Rick Schillo, RN, from Holy Family Hospital in Des Plaines; and two other nurses, Kathy Schillo, RN, and Barb Cerwyn, RN, from Northwest Community Surgicenter in Palatine. Pitman's wife, Kim, provided crucial support to the surgical team. The team also included Susan Dickson, executive director of the Foundation for Children's Reconstructive Surgery. The team operated on 25 children, many of whom needed multiple procedures, for four and a half days.

Like his colleague Michael Schafer, MD, Bradley got hooked on missionary work through Operation Rainbow. He views the India missions as a way to stir up resources to help doctors there do more to treat cleft lips and palates. "The important thing is that we stimulate interest and get eager people to help these children early on, or else nothing will get done," Bradley says.

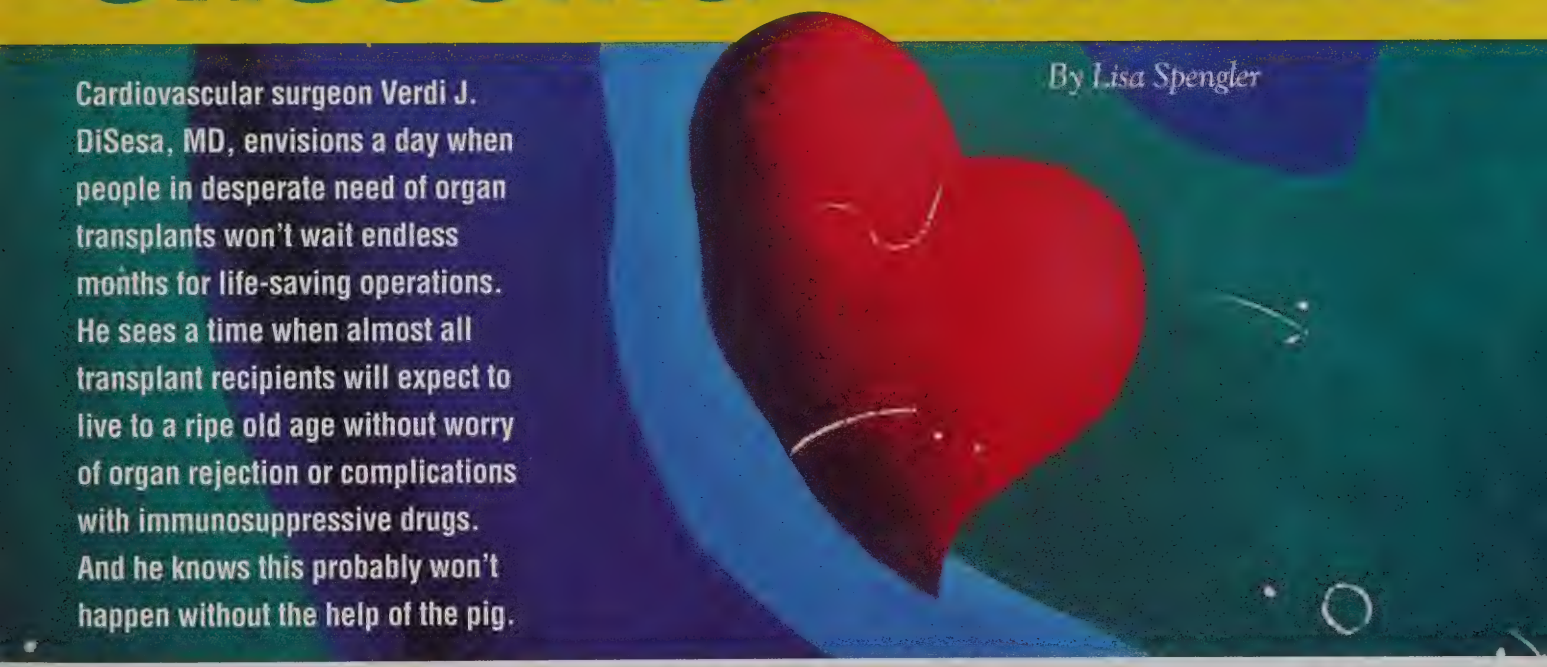
While patients and families are extremely thankful for the work Bradley and his team have done, it's not praise that fuels Bradley's missionary work: It's the love of his craft.

"It's hard to accept any praise for something that makes you feel that good. In fact, it feels kind of selfish," Bradley says. "When I have been on missions with friends, I'll watch an excellent surgeon take the operation apart for the second or third time just to make it a little more perfect, even when no one is judging it as critically as he is, or even knows who he is. On these missions, you see people doing their absolute best because that is what they love to do."

"IT'S HARD TO ACCEPT ANY PRAISE FOR SOMETHING THAT MAKES YOU FEEL THAT GOOD. IN FACT, IT FEELS KIND OF SELFISH."

— CRAIG BRADLEY, MD

CROSSING BARRIERS



Cardiovascular surgeon Verdi J. DiSesa, MD, envisions a day when people in desperate need of organ transplants won't wait endless months for life-saving operations. He sees a time when almost all transplant recipients will expect to live to a ripe old age without worry of organ rejection or complications with immunosuppressive drugs. And he knows this probably won't happen without the help of the pig.

By Lisa Spengler

Science hasn't discovered a miracle drug derived from the pig. But researchers, DiSesa included, have determined that pigs may someday be perfect organ donors for humans — perhaps an even better source of donor organs than humans themselves.

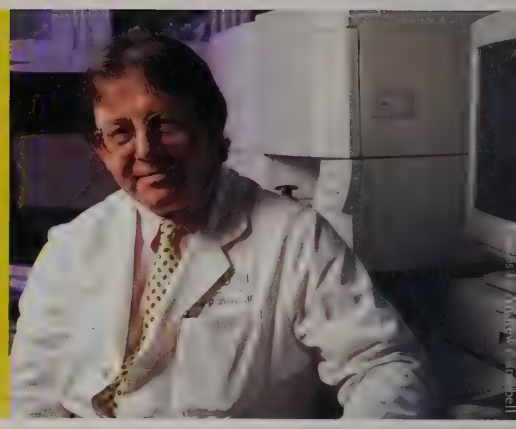
"Heart transplantation is an effective treatment for seriously ill people. But it doesn't take long to realize that we can't meet the enormous demand for donor organs," says DiSesa, who is surgical director of the Rush Heart Institute. "There's a shortage of donor organs. Hundreds of people die while waiting for transplants."

Each year, nearly 7,000 Americans await the chance to get a heart transplant. Only about 2,300 of them will get that crucial second chance at life. And that's just the estimated number of people waiting for hearts. Thousands more wait for other organs, such as livers, kidneys, lungs or pancreases.

Because of the overwhelming need to find another way to help patients waiting for life-saving transplants, scientists are looking into the prospect of using animal organs for human transplant. This xenotransplantation, as it is known, could solve the problem of organ donor shortages as well as other difficulties posed by human-to-human transplant, saving thousands of lives.

Cells and tissue from pigs are already being used to treat a wide variety of diseases. Until synthetic human insulin was introduced in the 1980s, people with diabetes were dependent upon insulin derived from animals, including pigs. Some patients who have defective heart valves have benefited from pig heart valve transplants. Nerve cells taken from pigs are being used to treat patients with Huntington's disease and Parkinson's disease. More recently, Rush became the

"IT DOESN'T TAKE LONG TO REALIZE THAT WE CAN'T MEET THE ENORMOUS DEMAND FOR DONOR ORGANS." — Verdi J. DiSesa, MD



first site in Chicago to study the effectiveness of a "bioartificial liver." The HepatAssist Liver Support System, used in conjunction with traditional medical treatments, can prolong the lives of patients in acute liver failure. The system uses cartridges of live pig liver cells to provide essential liver functions until a donor organ is found.

Refining an Old Idea

Xenotransplantation isn't a new idea. In fact, researchers have been investigating it since the turn of the century. Some surgeons have already taken the concept of xenotransplantation out of the laboratory and into the operating room. In 1985, the much-publicized case of Baby Fae, a newborn who received a baboon heart that kept her alive for 20 days, was the first instance of a heart xenotransplantation in an infant.

There also have been attempts to transplant primate livers and kidneys into humans. But these attempts have met with little success.

The main reason these animal-to-human transplant operations haven't saved lives is the same reason that some human-to-human transplants fail: organ rejection. Organ rejection occurs when a transplant recipient's immune system, the complex mechanism that enables the body to fight infection and disease, recognizes the donor organ as a foreign object and attacks it. Organ rejection is even more severe when transplants are performed between different species, such as in pig-to-human transplants.

To combat organ rejection in human-to-human transplants, doctors prescribe a cocktail of powerful drugs that slow down the immune system so donor organs can thrive unharmed. While these drugs do quell a violent immune response, they also cause side effects, such as hypertension and diabetes, and may even make patients susceptible to some cancers. Immunosuppressive drugs also leave transplant patients open to life-threatening infections.

DiSesa thinks the key to sidestepping the severe immune response in transplantation is to tailor each patient's immune system so that the person's body will tolerate a specific donor organ. This may be possible by mixing the donor's and the recipient's bone marrow before the organ is transplanted. Bone marrow is a major source of blood cells and, therefore, the source of many of the cells that activate the immune response. Theoretically, once the recipient has some of the donor's bone marrow, his or her body will be better suited to accept an organ from that same donor.

Tailoring the Immune System

Unfortunately, this method is extremely difficult with human-to-human transplants, because donors are usually identified only hours before transplant. But with the use of animal organs, donors could be identified well in advance, theoretically enabling physicians to orchestrate nearly ideal circumstances to reduce the chance for rejection.

DiSesa and his colleagues at Rush have tested this method with mouse-to-rat heart transplants with good results. The mouse heart, which is grafted to the rat's heart, survives much longer when the transplant is done with the bone marrow procedure. But, even though mixing donor and recipient bone marrow improves the chances of survival for transplant recipients, fundamental immunological differences between species still inhibit successful xenotransplantation surgeries.

Nevertheless, structural and functional similarities between pig organs and human organs make pigs good candidates for donors. A handful of experimental labs in the United States and Europe are breeding genetically engineered pigs designed to discourage organ rejection by human recipients. Uri Galili, PhD, an internationally known researcher whose arrival this year furthers Rush's reputation as a world-class center for xenotransplantation research, is working to produce a pig that lacks the cells that trigger the human immune response. The technology is still in early development, but these pigs will almost certainly play an important role in successful xenotransplantation.

Besides the immunological rejection barriers, there is a very real threat that xenotransplantation could introduce animal diseases into the human population. People tolerate many microorganisms that remain inert in humans. Similarly, pigs carry viruses and other organisms that don't harm pigs. But if a "harmless" pig virus is injected into a human, there's a chance it could make that person very ill. The Ebola virus and the human immunodeficiency virus (HIV) are examples of organisms that cause no harm to nonhuman primates such as baboons or monkeys. But once these viruses invade the human body,

they disturb vital organ functions and usually kill their host. "These animal-to-human infections definitely need to be studied," DiSesa says. "The last thing we want to do in xenotransplantation is to start an epidemic of pig viruses in humans."

Several well-respected scientific organizations have reviewed the advantages and disadvantages of xenotransplantation research. Most of these groups, including the U.S. Food and Drug Administration, have concluded that the risks of transspecies transplants are outweighed by the need to investigate alternatives to human-to-human transplants.

Establishing Guidelines

But that doesn't mean that xenotransplantation research goes unchecked. Hospitals and scientific organizations regulate all animal research. And when research studies reach the stage where human subjects are required, guidelines are extremely rigid.

While DiSesa and other researchers believe xenotransplantation is still at least a few years away from becoming a viable alternative to human-to-human transplantation, scientists are already proposing ways to monitor all stages of xenotransplantation research. DiSesa hopes to collaborate with Rush specialists in immunology, infectious disease, hematology, medical ethics and other specialties to identify and overcome the barriers.

If xenotransplantation does become a reality, some experts suggest that tissue samples should be collected from all donors and recipients so that any abnormalities or viruses can be traced. Researchers also think that the first xenotransplant recipients should be closely monitored to avoid the potential spread of disease and to track any other complications.

As researchers continue to confront these barriers, it becomes more and more clear that xenotransplantation has the potential to save thousands of lives. "Patients who, for whatever reason, weren't considered candidates for human organ transplantation may be perfect candidates for xenotransplantation," DiSesa says. "We could potentially eliminate the organ donor shortage problem."

So while it's true that pigs can't fly, they may someday do something much more impressive. ■

A PIECE OF THE FUTURE

Xenotransplantation is still off on the horizon, but xenografting, in which animal tissue is used to replace tissue in human patients, is already benefiting many people, including a woman recently treated at Rush.

A few years ago, Noreen Byrne, then in her late-60s, complained to her doctor about shortness of breath. "Also," she adds, "I just wasn't feeling as peppy as I used to."

Testing revealed that her aortic valve, which opens to allow blood to flow from the left ventricle of the heart into the aorta and on to the rest of the body, was abnormally small. After years of working harder to push the blood out, Byrne's heart had become enlarged — and she was feeling the strain.

In May of 1998, Byrne came to Rush to have the valve replaced.

"The whole point of aortic valve replacement is to get the best flow with the least amount of work for the heart," says Robert March, MD, director of cardiovascular research at the Rush Heart Institute, who performed Byrne's procedure.

Consulting with Byrne, March chose a stentless porcine valve. This valve is specially harvested, for the purpose of grafting, from a pig — the animal with a heart valve most similar to that of humans.

Surgeons have been using pig valves as xenografts, in one form or another, since the 1960s. The valves used today offer better blood flow than artificial devices, eliminating the need for a lifelong regimen of blood thinners — one of Byrne's concerns. Over time, the xenograft valves have been shown to improve both the functioning and condition of the heart, translating into longer patient survival and improved quality of life. Plus, not having to rely on the availability of human tissue — an option known as a homograft — means that the procedure can be performed under optimal conditions, with a range of valve sizes to choose from.

The results of Byrne's graft couldn't have been better. A postoperative echocardiogram could detect no difference between her healthy pulmonary valve — the aortic valve's closest cousin, which helps regulate blood flow from the heart to the lungs — and the xenograft valve.

"The flow through both valves," March says, "is now perfectly smooth."

In other words, a perfect match.

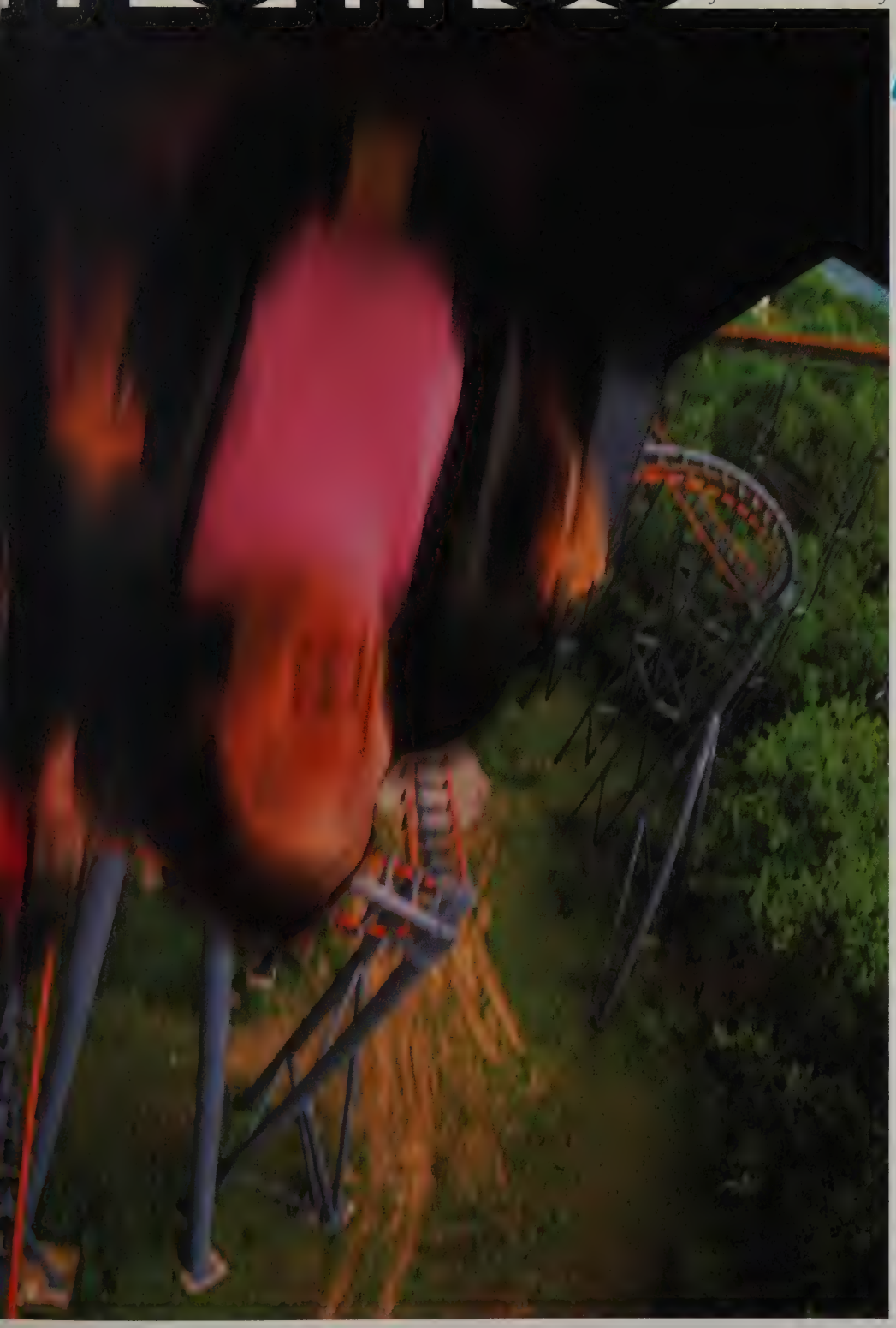
—Sean Carr

A Life of Ex

People with bipolar disorder — sometimes called manic-depressive illness — endure mood swings from dizzying highs to paralyzing lows. Mental health professionals at Rush are helping to create treatment guidelines for this terrifying illness.

tremes

by Marie Mahoney



Joanne saw the first signs of mental illness more than three decades ago, when she was a young mother at home with two small children. She remembers times when she was so low she didn't have the energy to open a can of soup. There were other times — like when she took an out-of-control joy ride in the middle of the night — when she felt so good she nearly killed herself.

Like an estimated 2 million other Americans, Joanne suffers from bipolar disorder. Sometimes referred to as manic-depressive illness, bipolar disorder is characterized by mood swings from dizzying highs to paralyzing lows.

"When they're manic, many people feel on top of the world, as if nothing bad can happen to them," says John M. Zajecka, MD, clinical director of the Woman's Board Depression Treatment and Research Center at Rush. "But eventually the bottom falls out. And when they drop, patients rarely drop to baseline. They drop quickly and deeply into depression.

"Treating bipolar depression is our biggest clinical challenge today," Zajecka says. "The last few years have seen a revolution in treatment options for mania and its milder form, hypomania," he says. "But there are currently no approved treatments for bipolar depression."

Zajecka is leading an effort at Rush to establish treatment guidelines for this forgotten aspect of bipolar disorder. The backbone of these guidelines are practice-based data on how patients respond to various treatments, collected by Zajecka and his colleagues in the Rush Institute for Mental Well-Being over the last three years. The project is supported by a grant from the Stanley Foundation, a private foundation with ties to the National Alliance for the Mentally Ill.

People with bipolar disorder ride an emotional roller coaster. When the ride ends, it ends with a crash.

A bumpy ride

When they're high, many people with bipolar disorder have an exaggerated sense of their own abilities, often to the point of believing they have superhuman powers. They talk nonstop. Sleep is beside the point. They often lose sight of the consequences of their actions. Sexual promiscuity is common, happy relationships less so.

Many people with the illness find that their moods swing at regular intervals from mania to depression, with episodes lasting several months or so. Others cycle at breakneck speed from one pole to the other — sometimes within the course of a day. Others spend much of their time in mixed moods, in which hopelessness and despair exist in an uneasy jumble with feelings of restlessness, anxiety and an overpowering impulsiveness. For people in this state, the risk of suicide is high.

When the ride ends, it ends with a crash. One business executive, who rode the manic-depressive roller coaster through several jobs in corporate finance over the course of a decade, says his depressions left him completely drained. "Projects I had been extremely enthusiastic about suddenly felt like drudgery," recalls the man, who has been stable for eight years or so on his current treatment.

No one knows precisely what causes these cycles. Scientists believe the illness is the result of an imbalance in certain neurotransmitters in the brain that regulate emotions. In this sense, bipolar illness resembles unipolar depression, the clinical name for the illness people generally think of when they hear the word "depression."

But bipolar disorder differs from its psychiatric cousin in an important respect. Many people have single episodes of so-called unipolar depression, although the likelihood that depression will recur increases with subsequent episodes. "But in all cases, bipolar illness is a chronic disease requiring lifelong medical treatment," Zajecka says.

Leveling the highs, lifting the lows

Since the late 1960s, the gold standard for treating bipolar disorder has been lithium, a naturally occurring element that acts as a mood stabilizer. Within the last five years or so, lithium has been joined by anticonvulsants such as the medication Depakote that also seem to help control manic symptoms. Even more recently, psychiatrists have found that certain medications known as atypical antipsychotics help control symptoms in some patients. "We call these atypical because they have a different mechanism of action than traditional antipsychotics," Zajecka says. "They seem to be better tolerated and appear to have a broader range of efficacy, treating mania as well as psychosis, symptoms that frequently overlap." These medications can help stabilize some patients whose manias are accompanied by psychotic symptoms, such as delusions and hallucinations.

Taken singly or in combination under the supervision of an experienced psychiatrist, these medications control manic symptoms in most patients. The treatment of bipolar depression is less straightforward.

The Genetics of Bipolar Disorder

Mike, a north suburban businessman, knows the clinical name for his illness — it's called bipolar disorder. But for him, it also goes by another name: the family sickness.

Mike knew that his father, who left home when Mike was a teenager, suffered from the illness. But it wasn't until some years after he started noticing symptoms himself that he learned his father was one of a long line, going back as far as anyone can remember.

Scientific studies have supported the hypothesis that bipolar disorder is genetically transmitted — that is, that the disease runs in families. But so far, none have identified the specific gene, or combination of genes, that predispose people to developing the illness, says William Scheftner, MD, medical director of the Rush Institute for Mental Well-Being.

Scientists involved in a multicenter study sponsored by the National Institute of Mental Health hope to crack the code. Rush is one of 10 U.S. medical centers participating in the study.

The study will recruit pairs of siblings diagnosed with bipolar disorder. These people will undergo clinical interviews about their symptoms, their family histories and their medical histories. Researchers also will ask participants about what physicians call comorbid conditions — conditions such as substance abuse, panic disorder and other mental illnesses that often accompany a diagnosis of bipolar disorder.

These interviews, along with DNA samples from participants, will be available for study by scientists nationwide, says Scheftner, who is the principal investigator of the study at Rush. "Three or four years from now we hope to begin using these data to seek clues to the genetic basis of bipolar disorder," he says.

"Some patients take lithium alone and are stable for many, many years," Zajecka says. But this is not always enough to stave off depression.

And though bipolar depression may symptomatically resemble unipolar depression, the two conditions cannot be treated the same way.

"If doctors treat bipolar depression as they would unipolar depression, it can result in a more severe presentation of the bipolar illness," Zajecka says. In bipolar patients, the use of antidepressants can bring on manic, hypomanic or mixed episodes, and can cause cycles to accelerate, leaving people with fewer — and shorter — periods of feeling normal.

That creates a quandary for physicians who treat patients with bipolar disorder. "If you polled psychiatrists, many would say you shouldn't prescribe antidepressants for bipolar patients," Zajecka says. "But these people are suffering, many of them with depressions worse than people with unipolar depression."

The gap in information on treating this aspect of bipolar disorder gave rise to the Stanley Foundation Bipolar Depression Consensus Group at Rush. The group has created a set of guidelines, based on clinical experience with more than 200 patients, for diagnosing and treating depression in bipolar patients. The guidelines offer suggestions on how to use antidepressants effectively within a medication regimen that includes mood stabilizers, alternative treatments such as light therapy for people whose illness varies with the seasons, and established treatments such as electroconvulsive therapy — or ECT — which has proven effective for many patients who haven't responded to medical interventions.

The consensus group — which includes Rush psychiatrists, psychologists, nurses and researchers — represents a novel approach to the problem. "We have several controlled medication studies under way in the treatment and research center, many of them involving

Photo by Jean Clough

John M. Zajecka, MD, is leading an effort at Rush to create treatment guidelines for bipolar depression.

medications for bipolar disorder," says Zajecka. "These studies necessarily subject patients and physicians to a number of artificial constraints — for instance, patients have to be off all other medicines and are quite often excluded if they have any other medical problems.

"Our idea with this study was to look at the illness in a real-world setting," Zajecka says. "We wanted to look at how a psychiatrist in the community would treat the illness, as opposed to how we would do it in the controlled setting of a clinical trial."

The critical data in this study have been supplied by the patients themselves. Using a tool called a life chart, patients keep track of how their moods change from day to day and rate their ability to function at home, work and school. Life charts have been used in a modern clinical setting only within the last decade. The idea was inspired by the work of the German psychiatrist Emil Kraepelin, MD, who used similar charts in the 1920s to track the natural course of mental illnesses such as bipolar disorder and schizophrenia before the advent of medical therapy.

Detailed study of these life charts has allowed the consensus group to create an algorithm of sorts to aid physicians in creating individualized treatment plans for their patients.

The guidelines take into account whether patients suffer from what physicians call "comorbid conditions" — illnesses that may accompany bipolar disorder. For instance, many people with bipolar disorder also struggle with problems such as alcoholism or substance abuse, attention deficit/hyperactivity disorder or other psychiatric problems.

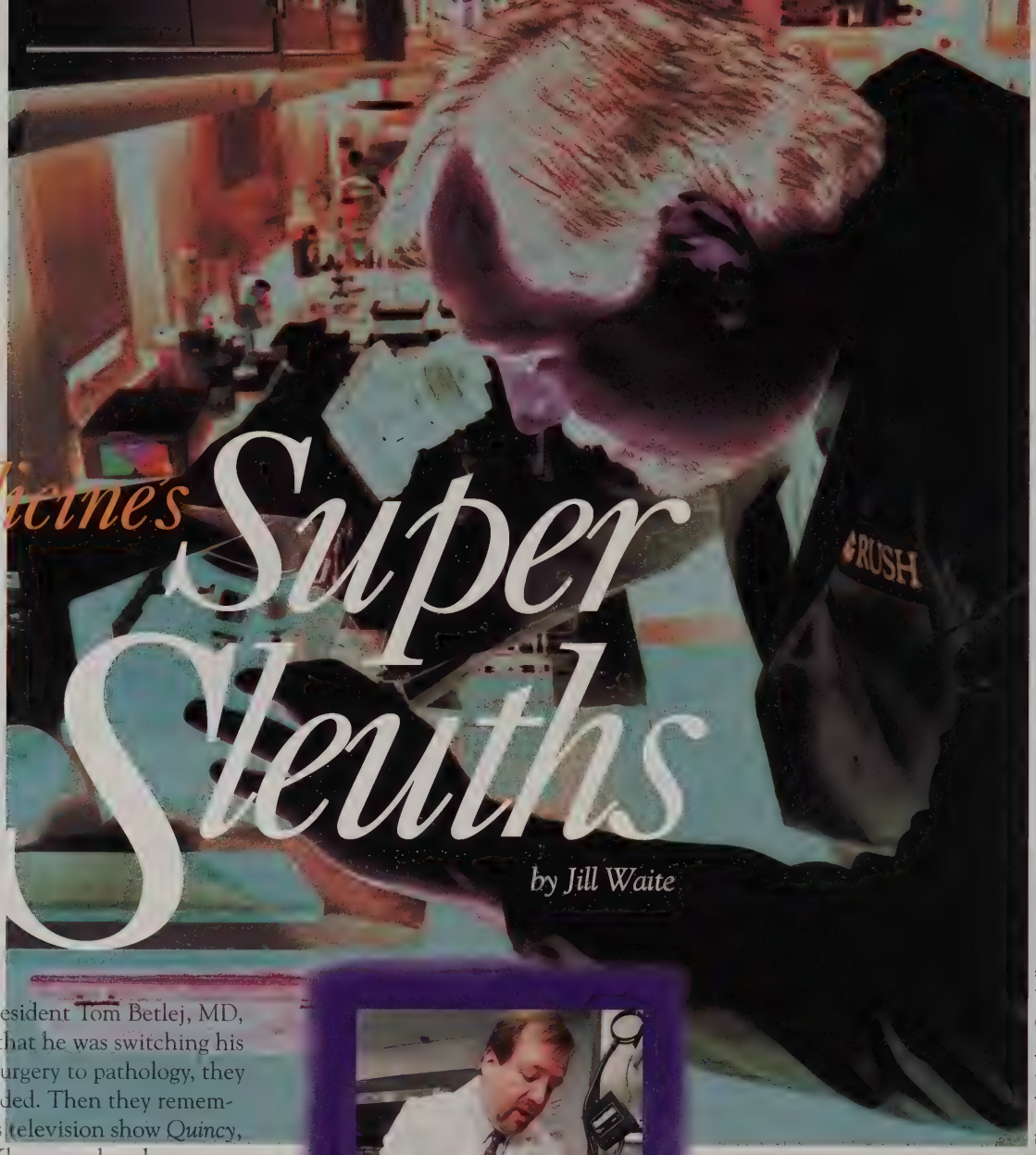
"Bipolar disorder is extremely heterogeneous," Zajecka says. "You could almost say there are as many manifestations of the disease as there are sufferers."

For that reason, the group does not intend for their treatment guidelines to be seen as a cookbook.

"We can't cure bipolar illness, but there is very little we cure in medicine," Zajecka says. "Unless you can cut it out or give an antibiotic for it, what we're really talking about is keeping disease under control. For people with bipolar illness, what we're aiming to do is help keep them firmly within a middle zone between the extreme highs of manias and the depths of depression. We hope our guidelines serve as a practical tool to help physicians get and keep their patients within that range." ■

Medicine's Super Sleuths

by Jill Waite



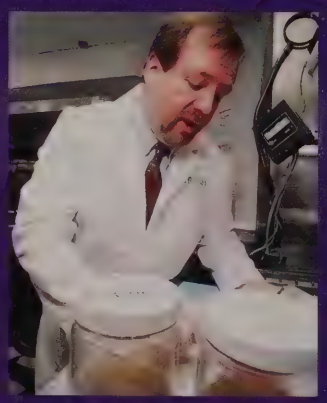
Photos by Andrew Campbell

When Rush resident Tom Betlej, MD, told his family that he was switching his specialty from surgery to pathology, they were dumbfounded. Then they remembered the 1970s television show *Quincy*, in which Jack Klugman played a super sleuth forensic pathologist. From the autopsies he performed, Quincy gathered incriminating evidence such as the poison contents of a victim's last meal, the point of entry of a deadly bullet or the mysterious substance under a victim's fingernails. With these discoveries, he fought crime and caught the bad guys all in an hour.

Betlej had to explain that *that* wasn't *exactly* what his job would be like.

Unlike Quincy, Betlej wouldn't be chasing murderers or working as a public official at a morgue. In fact, he wouldn't even be performing all that many autopsies. Instead, most of Betlej's days at Rush would be spent looking under microscopes, evaluating tissue samples, body fluids and cells.

The job description may not seem glamorous to some, but it's a profession that carries its own brand of excitement and intrigue. Pathologists here may not hunt down gun-toting killers, but they do play a vital role in smoking out such killers as cancer, heart disease, AIDS and other perpetrators such as hepatitis, lupus and the causes of transplant rejections.



The field of pathology may not seem glamorous to some. But it's a profession that carries its own brand of excitement and intrigue.

Equipped with high-powered microscopes, a wide array of colorful stains and some cutting-edge computer software, pathologists investigate the cause and nature of disease by examining structural and functional changes in the patient that suggest the presence of disease. Every time a biopsy or Pap smear specimen is obtained from a patient in an operating room or a doctor's office, it goes to the pathology lab. It's the pathologist's job to identify in the specimen anything from a viral infection to a benign mass to a malignant tumor.

How cancer is diagnosed in the pathology lab has changed dramatically, making the pathologist an integral part not just of the diagnostic process but of

the treatment as well. "Fifteen years ago a pathologist would say it was cancer and stop. Now it's just the beginning of what we do," says Kenneth J. Bloom, MD, director of operations for pathology. Thanks to techniques in the pathology lab that have revolutionized the study of disease, pathologists can now identify the cancer type and provide valuable prognostic information such as a cancer's stage of development.

As any pathologist knows, all cancers are not created equal. Each has a unique set of molecular characteristics that govern its behavior in different ways. A technique called immunohistochemistry allows pathologists to see how cells are structured and how they act. Other advances such as flow cytometry, a technique that forces cells through a light beam one at a time, and in situ hybridization have enabled pathologists to look at disease on a genetic level. This information helps predict how aggressively a cancer will spread, dictates the kind of treatment the patient will receive and opens doors for unexplored methods of cure by showing what cancers respond best to which types of treatment.

Every day, researchers depend on pathology to help guide them toward finding a treatment or cure — not just for cancer, but for other diseases as well. For example, Rush's experimental pathology researcher and director of electron microscopy, Jerome Kuszak, PhD, and his colleagues have traced how a normal eye lens evolves into one with a cataract by using high-tech magnification devices like an electron microscope and some cutting-edge computer wizardry. Understanding the anatomy of a healthy lens and that of a lens with cataracts has helped develop experimental treatments. "In disease you need to identify what is right to determine what went wrong," Kuszak says. "Once you do that, you can experiment with various drugs and dosages so that you can make it right again."

Pathologists are also the medical auditors at Rush. They check every placenta from every baby born at Rush to identify signs of developmental problems, and they count every screw and every plate removed from orthopedic patients during surgery to ensure that they were all taken out. Pathologists at Rush also examine every donor organ in Illinois for the regional organ transplant bank. Their evaluation determines what organs will be used for transplantation in hospitals all over the state.

Still, there are those autopsies. Twenty years ago, hospitals were required to perform a certain number of autopsies each year. Today, that is no longer the case. Revised guidelines from the Joint Commission on Accreditation of Hospitals and Healthcare Organizations, combined with better diagnostic tools, have lightened the autopsy workload at Rush.

But that's not to say that autopsies, and the doctors who perform them, aren't important. "Autopsy is the quality control of medicine," says John R. Dainauskas, MD, director of autopsy pathology. "It tells us if a clinical diagnosis was correct, identifies any undiagnosed conditions and shows us the effects of treatment." Information that pathologists obtain at autopsy can save lives by helping doctors improve their diagnostic abilities and therapeutic approaches.

Quincy never helped perfect a new drug or identify a hidden infection that saved a patient's life, nor did he make someone's day by finding out that, "no, it isn't cancer." If he did, those episodes are hidden in a vault somewhere in Los Angeles. Tom Betlej, now the chief pathology resident at Rush, and his colleagues, though, have a chance to do those things every day. They may not be TV detectives, but they do find the clues that solve medical mysteries. ■

Every day, researchers depend on pathology to help guide them toward finding a treatment or cure — for cancer as well as a host of other diseases.

Three-dimensional computer-aided designs help researchers visualize the anatomy of cataracts.

The virtual classroom

Last fall, Daniel Seltzer joined his family to celebrate Yom Kippur. Rather than watch a baseball game while he played with his baby daughter Amanda and waited for his mother and wife to finish dinner preparations, Dan decided to check out his health care ethics class at Rush University. And he took Amanda with him.

But Dan and Amanda didn't have far to go, thanks to Rush's new distance-learning program, which allows students to participate in classes from their computers. He attended his class right there in his mother's apartment.

Photo: Jean Clough

Daniel Seltzer with his wife and daughter.

Rush University began its journey into cyberspace education last year when Rush's McCormick Education and Technology Center collaborated with the Department of Religion, Health and Human Values to develop an online course.

In the fall of 1998, students from as far away as Texas and as close as the Rush campus participated in Rush's first virtual classroom, where tools such as e-mail, bulletin boards and chat rooms allowed students to enjoy the educational experience of a lecture hall without the hall itself.

The way it worked was simple. Instructors posted lecture material and class assignments for each lesson on the Rush University web site. Students could then log on from any computer with Internet capabilities.

Each week instructors held chat sessions so that students could discuss individual cases without gathering in a traditional classroom. Students who couldn't make the session could obtain transcripts of the online conversation from the Rush University web site.

Last winter the College of Nursing added its own course to the distance learning program. It was a resounding success, says Mary Pabst, RN, an instructor at the College of Nursing.

"This environment offers a different dynamic than a face-to-face lecture," says Russell Burck, PhD, director of graduate studies in health care ethics. "Students exhibit more candor in their questions, and that can be empowering for them."

Pabst agrees. "Students are freer to ask and answer questions. They feel safer in their anonymity," she says.

For more information about Rush University's online courses, go to www.rushu.rush.edu/onlineclasses.

— Jill Waite

Korean nurses visit Rush

Photo: Andrew Campbell

This spring, 11 home health nursing students and one faculty member from the University of Korea came to Rush to learn how the United States teaches and practices home health nursing. A highlight of the group's stay was a reception at the Robert W. Sessions House of Rush University, hosted by Rush president and CEO Leo M. Henikoff, MD, and his wife, Carole. To celebrate the occasion, the Korean nurses dressed in traditional gowns normally worn only on wedding days and New Year's.

— Jill Waite

Jacobs named to Crown chair

Joshua J. Jacobs, MD, has been named the inaugural holder of the Crown Family Endowed Professorship in Orthopedic Surgery at Rush University.

Jacobs came to Rush in 1987 as a fellow in joint replacement therapy. His work has earned him many grants to study total joint replacement from the National Institute of Arthritis and Musculoskeletal and Skin Diseases of the National Institutes of Health.

He is a member of numerous professional societies, including the American Academy of Orthopedic Surgery. He serves on the editorial board of *New Developments in Medicine and Drug Therapy*, and is consulting editor for the *European Journal of Experimental Musculoskeletal Research*.

Photo: Penny Lawrence

Joshua J. Jacobs, MD

Rush's comparative research program accredited

Rush's Comparative Research Center has been granted full accreditation by the National Association for Assessment and Accreditation of Laboratory Animal Care International.

The association's endorsement acknowledges the Medical Center's commitment to humane treatment of animals used for research, says Thomas J. Welsh, DVM, PhD, director of the center.

Photo: Jean Clough

Thomas J. Welsh, DVM, PhD

The assessment process is voluntary and takes from six months to a year to complete. The association gave Rush's lab its approval last November following a site visit a few months earlier. The program will undergo evaluation every three years.

"The assessors look at everything from how the facility treats its animals to the detergent used on the floor and the temperatures maintained in the rooms," Welsh says. "They want to ensure that researchers are adequately trained to handle animals as they conduct their studies."

— Aaron O. Hall

Brennan takes reins as Trustees chair

Edward A. Brennan has been elected chair of the Rush Board of Trustees. A member of the board since 1986, Brennan joined the group's executive committee in 1996.

Brennan retired as chairman and chief executive officer of Sears, Roebuck and Co. in 1995. He serves on the board of several national corporations, including Morgan Stanley Dean Witter & Co., Allstate Corporation, AMR Corporation, Minnesota Mining & Manufacturing Company, Unicom Corporation, Dean Foods Company and the SABRE Group.

Photo: David Joel

Edward A. Brennan

Trott elected general trustee

Byron D. Trott has been elected a general trustee at Rush-Presbyterian-St. Luke's Medical Center. Trott is managing director of the investment banking group at Goldman, Sachs & Co., where he is responsible for the Midwest region and co-head of the Chicago office.

Byron D. Trott

Judy M. Bachelder, PhD, OTR, FAOTA

Margaret Faut-Callahan, DNSc, CRNA, FAAN

Julia M. Cowell, PhD, RN, FAAN

Virginia E. Maikler, PhD, RN

Medical Center names new department chairs

Four new department chairs have been named at Rush University.

Judy M. Bachelder, PhD, OTR, FAOTA, was named chairman of the Department of Occupational Therapy. Bachelder helped found the Kansas Head Injury Association and the Independent Living Center, an organization that helps the disabled become more self-sufficient.

Julia M. Cowell, PhD, RN, FAAN, was appointed chair of the Department of Community and Mental Health Nursing. She previously was associate professor and served as interim department head of public health nursing at the University of Illinois at Chicago. Cowell's research emphasizes mental health concerns in school-aged children, especially immigrants and refugees.

Margaret Faut-Callahan, DNSc, CRNA, FAAN, was appointed chair of the Department of Adult Health Nursing. Since receiving her doctorate in nursing at Rush in 1989, Faut-Callahan has directed the Nursing Anesthesia Program, rated the top program of its kind by *U.S. News and World Report*.

Virginia E. Maikler, PhD, RN, was appointed chair of the Department of Maternal-Child Nursing. Maikler previously was an associate professor of maternal-child nursing at Rush and served as the department's associate chairperson for education. She is known for her research on pain management in children.

— Judy Grossman

Staying the course: Rush researcher helps heart patients follow doctors' orders

Ignoring doctors' recommendations about medications, exercise and lifestyle changes results in tens of thousands of deaths each year, increased hospitalizations and delayed recovery from illness, according to the American Heart Association. This noncompliance is a particular problem with heart patients, and costs the nation $76 billion annually in unnecessary medical expenses and lost productivity.

Albert Bellg, PhD, a cardiac psychologist at the Rush Heart Institute, has undertaken several studies to determine exactly why patients ignore doctors' advice and to identify ways that health care professionals can stop this from happening.

Bellg, in collaboration with cardiologist Robert Rosenson, MD, has zeroed in on cardiac rehabilitation patients in Rush's Preventive Cardiology Center, patients who have undergone heart procedures ranging from angioplasty to bypass surgery. These patients have been "prescribed" anywhere from 12 to 40 sessions of cardiac rehabilitation, part of which entails supervised exercise on treadmills and stationary bikes.

Bellg says that 40 percent of these patients attend fewer than half of their scheduled sessions. To find out why, he has used questionnaires that measure such feelings as depression, anxiety and something called interpersonal sensitivity. "Interpersonal sensitivity is feeling that others are critical of you and that they don't like you," he explains.

What Bellg has found so far is that those who score high on the interpersonal sensitivity scale are the ones who are most likely to miss more than half of their scheduled rehab sessions. "These people may not feel comfortable exercising in public. They may think that they're being judged," Bellg says.

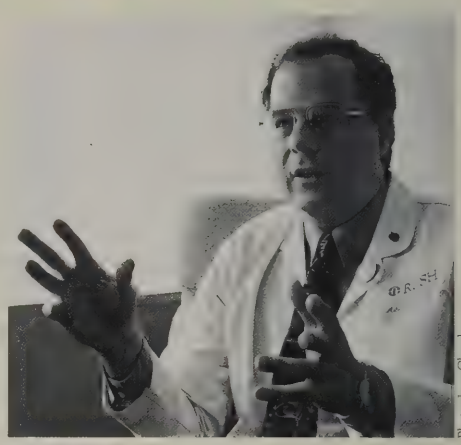


Photo: Jean Clough

Albert Bellg, PhD, a cardiac psychologist in the Rush Heart Institute

If the health care team is aware of this before rehab starts, Bellg believes they will be better equipped to help patients overcome these insecurities.

— Jill Waite

Rush physician lead author of stroke prevention guidelines

The National Stroke Association has issued the first comprehensive set of guidelines on stroke prevention. The information was published in the March 25 issue of the *Journal of the American Medical Association*. Neurologist Phillip B. Gorelick, MD, director of the Center for Stroke Research at Rush, was principal author of the guidelines, prepared by a panel of the nation's leading experts on stroke.

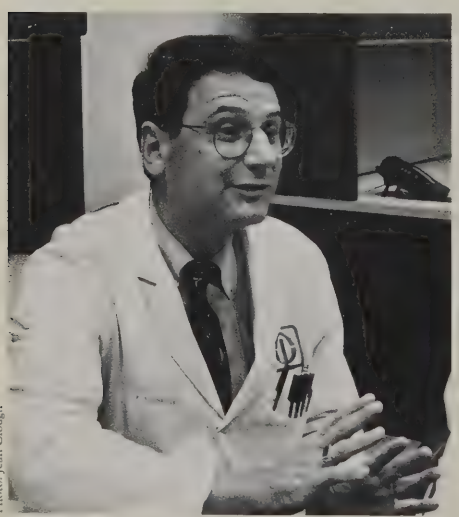


Photo: Jean Clough

Rush neurologist Phillip B. Gorelick, MD, was principal author of stroke prevention guidelines recently issued by the National Stroke Association.

Strokes occur when blood flow to the brain is abruptly cut off, usually by a blood clot that develops in or travels to an artery in the brain. As brain cells are starved of their lifesource — blood and the oxygen it carries — they wither and die. The devastating aftermath, from paralysis to loss of speech and memory, makes stroke the nation's leading cause of disability. Stroke, which claims more than 150,000 lives each year, is also the nation's third leading cause of death, exceeded only by heart disease and cancer.

"For the first time we have been able to give physicians a standardized way to manage patients and their risk for a first stroke," Gorelick says. "These guidelines are based on an extensive review and analysis of all existing information about risk factors and the incidence of stroke."

The guidelines focus on monitoring, controlling or preventing key risk factors for stroke. Medical conditions that place people at increased risk for stroke include high blood pressure, diabetes and high levels of cholesterol and other fats in the blood. Physicians can also help patients reduce their risk of stroke by encouraging them to cut down on alcohol consumption, eat a healthy diet rich in fruits and vegetables, and quit smoking.

The guidelines for physicians come fast on the heels of similar guidelines issued last year by the National Stroke Association to raise public awareness of the importance of stroke prevention. Says Gorelick: "We want physicians to have the most up-to-date information about stroke and its modifiable risk factors so that appropriate measures can be taken to prevent the first stroke from occurring."

— Marie Mahoney

New treatment may be alternative to chemotherapy for non-Hodgkin's lymphoma

A new cancer treatment, which uses a monoclonal antibody with a slight radioactive "tag" to shrink or destroy cancer cells, may provide an alternative to chemotherapy for patients with non-Hodgkin's lymphoma, according to researchers at the Rush Cancer Institute.

Rush is one of a number of U.S. academic medical centers participating in an expanded investigational study of the monoclonal antibody Bexxar, which is produced by Coulter Pharmaceuticals in Palo Alto, Calif.

Low-grade non-Hodgkin's lymphoma is an incurable cancer that affects the blood and lymphatic system. The National Cancer Institute estimates that approximately 270,000 people are afflicted with the disease, with an estimated 54,000 new cases diagnosed annually.

"Bexxar is a unique radiotherapy that combines monoclonal antibody technology with a radioactive isotope to direct treatment to the cancer cells," says Stephanie Gregory, MD, who is conducting the study at Rush. Monoclonal antibodies are sophisticated man-made versions of antibodies, the natural warriors produced by the body. Sophisticated technology allows laboratories to produce millions of identical copies of a single antibody that is specially designed to attack the same target.

Results from the initial study of Bexxar conducted at the University of Michigan were promising, Gregory says. About three-fourths of the patients enrolled in the study had a positive response to treatment, meaning most or all traces of cancer disappeared.

"The patients in this study had received an average of over four chemotherapy treatments before receiving Bexxar," Gregory says. "After treatment with Bexxar, the majority of the patients had a much longer period of time before the cancer reappeared, compared with chemotherapy treatment."

So far, four patients with low-grade non-Hodgkin's lymphoma have been treated with Bexxar at Rush. One patient, who was treated a year ago, remains in remission. Gregory says it is too early to evaluate the response of two patients who received treatment last October and one who was treated in January.

— Marie Mahoney

Photo: Andrew Campbell

Stephanie Gregory, MD, is leading a study at Rush on a new treatment for non-Hodgkin's lymphoma.

Bioartificial liver sustains patient awaiting transplant

A bioartificial liver at Rush kept a critically ill woman alive for seven days last January while doctors searched for a donor liver. Rush doctors were the first in Chicago to use a bioartificial liver to sustain a patient's life.

The 33-year-old patient, who asked not to be identified, left the hospital in mid-February after a month-long stay at Rush and resumed her normal life as a mother on Chicago's South Side.

"The machine allowed her to survive long enough so she could receive a transplant," says Lawrence McChesney, MD, a transplant surgeon and principal investigator of a research study examining the bioartificial liver's effectiveness.

The patient came to Rush acutely ill and close to death as a result of her liver failure. "Once the patient was connected to the bioartificial liver system, she received almost immediate relief from the most deadly symptom of liver failure, cerebral edema, or brain swelling," says Elizabeth Fagan, MD, a liver specialist and co-investigator of the study. "Since her transplant, she's recovered well, considering all odds were against her."

Investigators believe that the highly purified live pig liver cells the bioartificial liver uses can temporarily provide a patient with essential liver functions until a donor liver becomes available. The equipment, which resembles a kidney dialysis machine, accepts cartridges that contain the pig liver cells.

The machine passes the patient's plasma, which is separated from the blood cells, through fiber membranes that are surrounded by the pig liver cells. Molecules travel back and forth across the membranes, allowing the pig liver cells to work in a manner similar to that of a healthy human liver.

Researchers say the machine represents a major advance in helping patients with acute liver failure, given the continuing and increasing shortage of donor livers and the rapid progress of the disease.

Last year, the U.S. Food and Drug Administration approved randomized Phase II/III clinical trials of the Hepat-Assist Liver Support System, made by Circe Biomedical of Lexington, Mass., at six liver transplant centers worldwide —five in the United States and one in France.

— Laura Ramos

First Lady Hails Rush Epilepsy Center

First Lady Hillary Rodham Clinton visited Rush-Presbyterian-St. Luke's Medical Center on Jan. 13 to raise awareness about epilepsy, a central nervous system disorder that affects more than 2.3 million Americans, and to dedicate Rush's new six-room epilepsy monitoring unit in memory of Frank Morrell, MD, who founded the Rush Epilepsy Center in 1972.

Mrs. Clinton's visit was organized in part by the Epilepsy Foundation of America and Citizens United for Research in Epilepsy.

"The progress being made here is a tribute to the tireless efforts of the physicians, nurses and other staff members," Mrs. Clinton told a captivated audience of epilepsy patients, their families, Medical Center staff and members of the press. "We can all do something to help bring the day closer when there is no more ignorance about epilepsy, and, hopefully, when there is no more suffering. What better way to carry on Dr. Morrell's legacy than to commit ourselves to fulfilling the vision of hope that he established here."

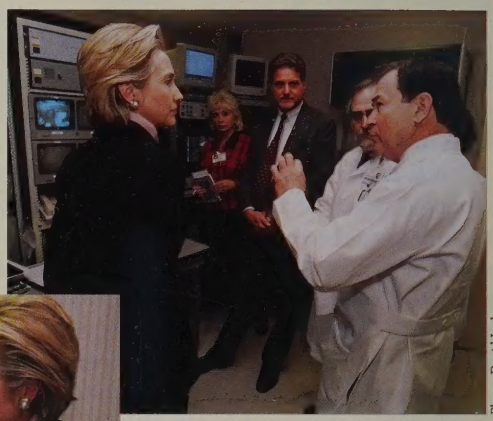


Photo: David Joel

Photo: David Joel

Photo: David Joel

Clockwise from top: Hillary Rodham Clinton with Rush president and CEO Leo M. Henikoff, MD, in the Epilepsy Monitoring Unit; Mrs. Clinton gets a warm welcome from Dr. Morrell's granddaughter, Anna Rose Morrell; Frank Morrell, MD, pictured a few years before his death, proudly displays the tooth given to him by a young patient; an epilepsy patient shares her experiences with the First Lady.

RUSH

Rush-Presbyterian-St. Luke's Medical Center
1700 West Van Buren, Suite 250
Chicago, Illinois 60612

address service requested

Non-Profit Org.
U.S. Postage
PAID
Chicago, IL
Permit No. 1207